50 YEARS OF THE DOUBLE HELIX

An anniversary of major medical interest passed by virtually unnoticed last month. On 2 April 2003 it was exactly 50 years since the publication of a letter in the journal *Nature* by James Watson and Francis Crick[1]. In it, they described the double helix molecular structure of deoxyribose nucleic acid (DNA) (Fig. 1), a publication which ushered in a new era in medicine. The two, a former ornithology student and an ex-physicist respectively, formed a most unlikely pairing. Crick, a Briton, still had no PhD at age 35. The American Watson, 12 years Crick's junior, had graduated from the University of Chicago at 19 and obtained his doctorate in ornithology at 22. Crick had migrated from physics into chemistry and biology, fascinated by the line 'between the living and the nonliving.' Watson had developed a research interest in viruses.

Robert Wright, author of *The Moral Animal: Evolutionary Psychology and Everyday Life*, writes[2]: 'On Feb. 28, 1953, Francis Crick walked into the Eagle pub in Cambridge, England, and, as James Watson later recalled, announced that "we had found the secret of life". Actually, they had. That morning, Watson and Crick had figured out the structure of the DNAmolecule. That structure—a "double helix" that can "unzip" to make copies of itself — confirmed suspicions that DNA carries life's hereditary information. Not until decades later, in the age of genetic engineering, would the Promethean power unleashed that day become vivid.'

The story of how it all came about is in itself fascinating. At a conference in Naples, Watson saw a vague, ghostly image of a DNAmolecule rendered by X-ray crystallography. DNA, he had heard, might be the stuff genes are made of. He viewed this as 'a potential key to the secret of life' and saw it as a career opportunity. Watson put his thoughts into a book in which he described his search for success in biochemistry and in particular, the race against Linus Pauling for the Nobel Prize that he thought DNA would surely bring, but the book got bad reviews from the (relatively) genteel Crick. However, they shared an interest in DNA, and when they found themselves in the same laboratory at the University of Cambridge, they started their collaboration. The rest is, as they say, history.

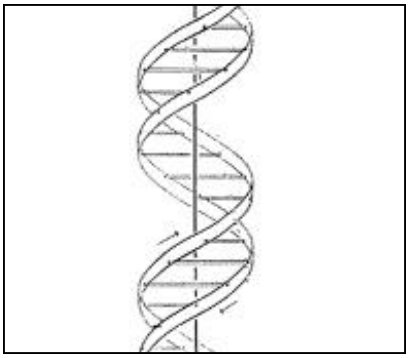

Fig 1: The double helix of DNA[4]

The pleasant atmosphere of Cambridge was not present in a laboratory at King's College, London. The strained atmosphere arose from the dislike between Maurice Wilkins, also working on DNAand Rosalind Franklin. This adverse relationship resulted in Wilkins performing a rather unethical act. Franklin was in the process of creating the world's best X-ray diffraction pictures of the DNA molecule. Unbeknown to Franklin, Wilkins showed one of her pictures, as yet unpublished, to Watson. According Robert Wright[2], 'The instant I saw the picture my mouth fell open,' Watson recalled. The sneak preview 'gave several of the vital helical parameters'.

Rosalind Franklin was a remarkable woman. She was not prepared to tolerate the treatment meted out to women at King's College [3]. Women were not readily accepted as individuals or scientists.. The women scientists were not allowed to eat lunch in the common room where the men did, for example. That and the strained relationship with Wilkins resulted in Franklin leaving King's College for Birkbeck College in London, where she headed her own research group. She was only let go from King's on the condition she would not do any further work on DNA. She turned her attention to viruses, publishing 17 papers in five years. Her group's findings laid the foundation for structural virology.

During a visit to the United States, Franklin experienced pain that originated from an ovarian cancer. She continued working over the next two years, despite operations and experimental chemotherapy. She had a 10-month remission, but eventually died in 1958 at age 37.

Robert Wright continues: In 1962 the Nobel Prize, which isn't given posthumously, went to Watson, Crick and Wilkins. In Crick's view, if Franklin had lived, 'it would have been impossible to give the prize to Maurice and not to her because she did the key experimental work.' She had also published a critique of an early Watson and Crick theory which sent them back to the drawing board. Her notebooks showed that she had been working toward the solution until Watson and Crick found it. She had narrowed the structure down to some sort of double helix. But she never employed a key tool—the big 3-D molecular models that Watson and Crick were fiddling with at Cambridge.

DNA's discovery has been called the most important biological work of the last 100 years, and the field it opened may be the scientific frontier for the next 100.

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2. *Wright R. James Watson and Francis Crick www.time.com/time/time100/scientist/ profile/watsoncrick03.html*
3. *A Science Odyssey. www.pbs.org/wgbh/aso/databank/entries/*
4. *Nature 1953;171:737.*